UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,809	03/13/2000	Michael P. Murphy	686.03.498CON	6553

7590 10/01/2004

Hollie L Baker
Hale and Dorr LLP
60 State Street
Boston, MA 02109

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/523,809	MURPHY ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *31-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 07/14/04 has been acknowledged.
Claims 53-64 are newly filed.
Claims 31-64 are pending and are examined in this office action.

*Applicants are required to follow Amendment Practice under revised **37 CFR §1.121.** The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 31-64 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the office action mailed on 03/10/04.

Nature of Invention:

Invention relates to an artificial skin construct.

Breadth of Claims and Guidance Provided in the Specification

The scope of instant claims encompasses:

A cultured skin construct having at least two layers, comprising: a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix in the absence of exogenous matrix components during the culturing conditions *(any and all: growth factor and culture conditions not defined)*; and (b) a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer, wherein the epidermal cell layer is multilayered, stratified, differentiated and exhibits a basal layer, suprabasal layer, a granular layer and a stratum

corneum; and wherein the bilayered cultured skin construct has a basement membrane present at the junction of the first and second layers (*wherein the keratinocyte cells makes an epidermal layer (as claimed) under any and all culture conditions: i.e. growth factors and culture conditions).*

A cultured skin construct having at least two layers, comprising: a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix in the absence of exogenous matrix components during the culturing conditions *(any and all: growth factor and culture conditions not defined)*; and (b) a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer *wherein the keratinocyte cells makes an epidermal layer (as claimed) under any and all culture conditions: i.e. growth factors and culture conditions).*

A cultured skin construct having at least three layers, comprising: a) a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix in the absence of exogenous matrix components during the culturing conditions *(any and all: growth factor and culture conditions not defined)*; and (b) a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer (*wherein the keratinocyte cells makes an epidermal layer (as claimed) under any and all culture conditions: i.e. growth factors and culture conditions)* c) and a third layer of cells deposed on the second layer.

In addition the scope of invention as claimed encompasses method of producing and using the above mentioned skin construct for transplantation or implantation into a patient.

Even though the specification teaches optimization of culture conditions for human fibroblasts to produce a layer of extracellular matrix in the absence of exogenous matrix components (see spec. Examples 1, 3 and 15), the specification fails to disclose what are the culturing conditions i.e. culture media contents, growth factors, culture environment that leads to the synthesis of (i) type I and type III collagen, (ii) decorin, (iii) fibronectin, (iv) tenascin, and, (v) glycosaminoglycans. Specifically, the specification fails to disclose a culturing condition (culture media contents, growth

factors, culture environment) in which the fibroblast cells when cultured produce type I and type III collagens (as claimed) and tenascin. The specification fails to identify type I and type III collagens (as claimed) and tenascin in the extracellular matrix secreted by cultured fibroblasts. In addition the specification fails to disclose that fibroblast cells derived form tissues selected from form tendon, lung, cartilage, urethra, corneal stroma, oral mucosa, umbilical cord, and intestine are capable of synthesizing extracellular components (as claimed) under any and all culture conditions. Regarding formation of an epidermal layer the specification only disclosed the use of a specific culture conditions, which comprises culturing the seeded keratinocytes in an epidermalization medium followed by culturing of the skin construct under submerged conditions (air-liquid interface) in a culture media that is different from the epidermalization medium (Spec. page 46, example-16). The specification fails to disclose that use of any and all culture conditions (i.e. culture media contents, growth factors, culture environment) would lead to the formation of an epidermal layer (as claimed) in a cultured skin construct.

State of Art and Predictability

The state of the tissue engineering art at the time of filing teaches that to engineer living tissues in vitro, cultured cells are coaxed to grow on bioactive degradable scaffolds that provide the physical and chemical cues to guide their differentiation and assembly into three-dimensional tissues. The assembly of cells into tissues is a highly orchestrated set of events that requires time scales ranging from seconds to weeks and dimensions ranging from 0.0001 to 10 cm. Coaxing cells to form tissues in a reliable manner is the quintessential engineering design problem that must be accomplished under the classical engineering constraints of reliability. Even though fewer than five engineered tissues have been approved, there are still many technical challenges to overcome before an "off-the-shelf" tissue could be created that represent the translation of scientific discoveries into treatments for patients. Furthermore, the successful large-scale production of engineered tissues requires an adequate source of healthy expandable cells, the optimization of scaffolds, and the creation of bioreactors, which mimic the environment of the body and that are amenable to scale-up. Additional

challenges include the preservation of the product so that it has a long shelf-life and the successful use of various approaches to prevent tissue rejection (Naughton et al Science 295:1009-1014, 2002).

Under the law Limitations appearing in the specification but not recited in the claim are not read into the claim. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). Furthermore, claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims. Raytheon Co. v. Roper Corp., 724 F.2d 951, 957, 220 USPQ 592, 597 (Fed. Cir. 1983), cert. denied, 469 U.S. 835 (1984). See also MPEP § 2111 - § 2111.01.

In instant case the invention as claimed encompasses multi-layered cultured skin construct comprising a layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix in the absence of exogenous matrix components during any and all culturing conditions. The instant claims fail to recite what are the culturing conditions for example culture media contents, growth factors, culture environment that leads to the synthesis of the claimed extracellular matrix components (I and type III collagens, decorin, fibronectin, tenascin and any and all glycosaminoglycans to support the growth and proliferation of second layer of epithelial cells. Similarly the instant claims fail to recite what are the culturing conditions (culture media contents, growth factors, culture environment that leads to the formation of epidermis during any and all culturing conditions.

Response to arguments

The applicant argues that the fact that the experimentation may be complex does not necessarily make it undue if art is typically engage in such experimentation. The applicant argues that the specification does teach one skilled in the art to how to make and use the invention without undue amount of experimentation. Regarding the culture media content and culture conditions the applicant argues that specification discloses various culture media and culture conditions like growth medium, production medium, epidermalization medium, cornification medium, maintenance medium, chemically defined medium, seed medium, and other medias. The applicant argues that the

specification discloses various examples that show the production of various cellular matrixes under various culture conditions and in the presence of various chemically defined medias.

However, applicant's arguments are found NOT persuasive. The invention as claimed encompasses multi-layered cultured skin construct comprising a layer of cultured dermal fibroblast cells, which produce a layer of extracellular matrix in the absence of exogenous matrix components during any and all culturing conditions. The invention as claimed fails to recite what are the culturing conditions for example culture media contents, growth factors, culture environment that leads to the synthesis of the claimed extracellular matrix components (I and type III collagens, decorin, fibronectin, tenascin and any and all glycosaminoglycans to support the growth and proliferation of second layer of epithelial cells. Similarly the instant claims fail to recite what are the culturing conditions (culture media contents, growth factors, culture environment that leads to the formation of epidermis during any and all culturing conditions. The earlier office action clearly provided the evidence that the assembly of cells into tissues is a highly orchestrated set of events that requires time scales ranging from seconds to weeks and dimensions ranging from 0.0001 to 10 cm. Coaxing cells to form tissues in a reliable manner is the quintessential engineering design problem that must be accomplished under the classical engineering constraints of reliability (see Naughton et al Science 295:1009-1014, 2002). Therefore defining culture conditions and a chemically defined medium required for each step involved in the development of cultured skin construct is considered essential practice the instant invention. Even though the specification discloses various chemically defined medias like growth medium, production medium, epidermalization medium, cornification medium, maintenance medium, chemically defined medium, seed medium, and other medias it is unclear which media is used at each step during the development of the cultured skin construct as claimed.

Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is

whether, given the Wands factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In instant case making a multi-layered cultured skin construct under any and all culture conditions (culture media contents, growth factors, culture environment) is not routine in the art and without sufficient guidance to a specific culture conditions the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

Claims 31-32, 36-38, 48-49 stand rejected under 35 U.S.C. 102(b) as being anticipated by Fleishmajer et al (J. Histochem Cytochem 41(9):1359-66, 1993), for the same reasons of record as set forth in the office action mailed on 03/10/04.

The instant claims are drawn to a cultured skin construct having at least two layers, comprising: a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix and a second layer of keratinocyte cells disposed on the first layer to form an epidermal cell layer, wherein the epidermal cell layer is multilayered, stratified, differentiated and exhibits a basal layer, suprabasal layer, a granular layer and a stratum corneum; and wherein the bilayered cultured skin construct has a basement membrane present at the junction of the first and second layers.

Fleishmajer et al teaches a keratinocytes-fibroblast co-culture model for reconstruction of human skin (see claims 31-32, 36-38). Regarding claims 48-49 the cited art teaches an isolation of fibroblast and keratinocytes from human neonatal foreskin. The cited art further teaches fibroblasts were seeded onto a nylon mesh (in the absence of an extracellular matrix) and were kept in culture for 26 days in a chemically defined medium comprising DMEM containing 10% calf serum and 100ug/ml ascorbic acid. The cited art further teaches that at the end of culture the fibroblasts were

embedded I a rich extracellular matrix that closely resembles the in vivo situation. The cited art further teaches that keratinocytes were seeded onto the dermal substrate comprising the cultured fibroblasts and grown submerged for one week, followed by second growth period in a air-liquid interface in a second culture medium comprising DMEM containing 5% FCS, 100 ug/ml ascorbate and 0.5ug/ml hydrocortisone (page 1359, col.2 para.2). In addition the cited art teaches that the keratinocytes-fibroblast co-culture model express extracellular matrix components: Type-I and Type-II collagen, Decorin (a glycosaminoglycan), Fibronectin and Tenascin (page 1365, table-I). Regarding claim 31 the cited art further teaches that keratinocytes-fibroblast co-culture model forms a basal lamina (basement membrane) at the junction between the keratinocytes layer and fibroblast cells comprising type-IV collagen, laminin, nidogen and heparan sulfate (page 1362, col.2, para.1). Thus the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that the cited art does not disclose a cultured skin or tissue construct that produces extracellular matrixes in the absence of exogenous matrix components. The applicant argues that the cited art teaches culturing fibroblast cells on a nylon mess and because of this distinction the cited art does not anticipate the invention as claimed.

However, applicant's arguments are found NOT persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the fibroblast are NOT seeded on nylon mesh) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The scope of invention as claimed is broad which clearly encompasses the keratinocytes-fibroblast human skin construct of Fleishmajer. Thus the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

Claims 33-35, 39-47 and 50-52 rejected under 35 U.S.C. 103(a) as being unpatentable over Fleishmajer et al (J. Histochem Cytochem 41(9):1359-66, 1993) as applied to claims 31-32, 36-38, 48-49 above, and further in view of Naughton et al (US 5,266,480, 1993) for the same reasons of record as set forth in the office action mailed on 03/10/04.

Claims 39-47 are drawn to a cultured skin construct having at least three layers, comprising: a first layer of cultured dermal fibroblast cells which produce a layer of extracellular matrix and a second layer of epithelial cells (keratinocytes) disposed on the first layer to form an epidermal cell layer, and a third layer of cells diposed on the second layer of epithelial cells. Claims 34-35 and 44-45 are drawn to fibroblast cells that are genetically engineered. Claims 33 and 42 are further drawn to a skin construct containing dermal papilla of hair follicles. Claims 50-52 are drawn to a method for transplantation or implantation of cultured skin construct in a patient.

Fleishmajer et al teaches a keratinocytes-fibroblast co-culture model for reconstruction of human skin (see claims 31-32, 36-38). Regarding claims 48-49 the cited art teaches an isolation of fibroblast and keratinocytes from human neonatal foreskin. The cited art further teaches fibroblasts were seeded onto a nylon mesh (in the absence of an extracellular matrix) and were kept in culture for 26 days in a chemically defined medium comprising DMEM containing 10% calf serum and 100ug/ml ascorbic acid. The cited art further teaches that at the end of culture the fibroblasts were embedded I a rich extracellular matrix that closely resembles the in vivo situation. The cited art further teaches that keratinocytes were seeded onto the dermal substrate comprising the cultured fibroblasts and grown submerged for one week, followed by second growth period in a air-liquid interface in a second culture medium comprising DMEM containing 5% FCS, 100 ug/ml ascorbate and 0.5ug/ml hydrocortisone (page 1359, col.2 para.2). In addition the cited art teaches that the keratinocytes-fibroblast co-culture model express extracellular matrix components: Type-I and Type-II collagen, Decorin (a glycosaminoglycan), Fibronectin and Tenascin (page 1365, table-I).

Regarding claim 31 the cited art further teaches that keratinocytes-fibroblast co-culture model forms a basal lamina (basement membrane) at the junction between the keratinocytes layer and fibroblast cells comprising type-IV collagen, laminin, nidogen and heparan sulfate (page 1362, col.2, para.1). However Fleishmajer does not teaches a third layer of cells deposited on the second layer of epithelial cells. In addition Fleishmajer does not teaches genetic motification of cell in keratinocytes-fibroblast co-culture model or a skin construct containing a dermal papilla of hair follicles.

Naughton et al teaches a three-dimensional skin culture system. Regarding claims 34-35 and 44-45 (genetically engineered cells) the cited art teaches genetic modification of cells used in the three-dimensional culture system to produce a foreign gene product selected from a growth factor, regulatory factor, peptide, hormone, antibody etc (co.20 lies 54-62). Regarding claim 39-41 and 43-47 (three layered skin construct) the cited art teaches a culture of isolated fibroblasts was established on a nylon mesh, which resulted in the adherent and growth of fibroblasts into the meshwork. The cited art teaches that these fibroblasts were metabolically active, secreted an extracellular matrix, and rapidly formed a dermal equivalent consisting of active fibroblasts and collagen (type I any type III) see col.44 lines 20-35. The cited art further teaches that melanocytes (second layer) were plated on to the fibroblast coated nylon mesh and allowed to grow for 3 days prior to the addition of keratinocytes (third layer) see col.45 lines 1-14. In addition the cited art teaches that other types of cells that may be used to inoculate the three-dimensional matrix include endothelial cells, pericytes, macrophages, monocytes, lymphocytes, plasma cells adipocytes etc (col. 30 line 53-59). Regarding claim 33 and 42 (hair follicles) the cited art teaches three-dimensional skin culture system may include introduction of a hair follicles and associated glands into the transplant site. The cited art further teaches implantation of skin-constructs containing hair follicles thereby creating a transplanted site, which is histologically normal and functionally similar to the normal skin (col.31, lines 44-59). Regarding claims 50-52 (method of transplanting) the cited art teaches a method for transplantation or implanting of cultured skin construct in-vivo (col.45, line 40). The cited art teaches transplantation of skin construct in experimental rats, wherein meshes with dermal and

epidermal components were implanted into 10mmx10mm skin biopsies. The cited art further teaches that these engraftment studies suggested that the three-dimensional skin matrix system mimics a true physiological system in which all cell components are activated and natural growth factors are being produced (col. 46 lines 8-24).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the teaching of Fleishmajer by substituting fibroblasts with genetically engineered fibroblast cells in view of Naughton. One would have been motivated to do so to produce recombinant protein in the skin construct (bioreactor system). Furthermore, it would have been obvious to one ordinary skill in the art to modify the skin construct of Fleishmajer by incorporating dermal papilla of hair follicles in view of Naughton. One would have been motivated to do so induce hair growth at site of skin implant. In addition a method for transplantation or implantation of a skin construct as taught by Fleishmajer is obvious in view of Naughton who teaches the technique of skin biopsies and transplantation. On would have been motivated to do so to promote wound healing in transplanted patients. One would have a reasonable expectation of success in doing so because genetic engineering of fibroblast host cells, substitution of a cell type in a skin construct and transplantation of skin construct is not only well within the reach of one ordinary skill in the art but also has been routine in the art.

Response to arguments

The applicant argues that there is no suggestion or motivation to combine the teaching of cited art. The applicant argues that Fleishmajer et al. does not disclose a cultured skin or tissue construct wherein the "extracellular matrix is produced by the cultured (dermal fibroblast cells in the absence of exogenous matrix components." The applicant argues that Naughton does not disclose the claimed invention and teaches away from the invention as claimed as it uses the exogenous matrix components.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in

the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Instant case the applicant fails to consider the combined teaching of the reference cited herein in entirety. Fleishmajer teaches a keratinocytes-fibroblast human skin construct modification of which to include a third layer of cells deposited on the second layer of epithelial cells and genetic modification of cell in keratinocytes-fibroblast co-culture is obvious in view of Naughton's disclosure.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the fibroblast are NOT seeded on nylon mesh) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The scope of invention as claimed is broad which clearly encompasses the keratinocytes-fibroblast human skin construct of Fleishmajer. In addition Naughton teaches a third layer of cells deposited on the second layer of epithelial cells and genetic motification of cell in keratinocytes-fibroblast co-culture model or a skin construct containing a dermal papilla of hair follicles. Thus invention as claimed is obvious, since one ordinary skilled in the art would be able to modify the teaching of Fleishmajer by substituting fibroblasts with genetically engineered fibroblast cells in view of Naughton with a reasonable expectation of success.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.** *Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to* ***(571) 272-0547.***

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER